Ventricular function after coronary artery bypass grafting: Evaluation by magnetic resonance imaging and myocardial strain analysis

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Objective: Magnetic resonance imaging with radiofrequency tissue tagging permits quantitative assessment of regional systolic myocardial strain. We sought to investigate the utility of this imaging modality to quantitatively determine preoperative impairment and postoperative improvement in ventricular function in patients with ischemic heart disease.

Methods: Magnetic resonance imaging with radiofrequency tissue tagging was performed on 6 patients (average age 60.2 ± 13.7 years) with coronary artery disease and 32 control subjects with no known heart disease. Patients with coronary artery disease underwent imaging before and 3 months after coronary artery bypass grafting. The ventricle was divided into 6 segments within a midventricular plane. Regional 2-dimensional left ventricular circumferential strain was calculated from tagged magnetic resonance images throughout systole. Circumferential strain results were compared in patients before and after and 3 months after coronary artery bypass grafting and also in control subjects.

Results: Before the operation circumferential strain identified 100% (10/10) of all regional wall motion abnormalities seen by preoperative ventriculography. Postoperatively, improvements were demonstrated in 56% (20/36) of the regions, and these improvements agreed with viability testing by single-photon emission computed tomography when available. Additionally, preoperative global circumferential strain for the ischemic group was significantly depressed relative to that in control subjects (0.11 ± 0.05 vs 0.20 ± 0.03, $P < .001$). Global circumferential strain correlated with ejection fraction by ventriculography ($r = 0.84$, $P < .01$) and improved after coronary artery bypass grafting (0.14 ± 0.05 vs 0.11 ± 0.05, $P < .01$).

Conclusions: Magnetic resonance imaging with radiofrequency tissue tagging permitted circumferential strain calculation. This technology quantitatively demonstrated improvements in left ventricular wall motion after coronary artery bypass grafting for both individual regions and the entire ventricle. This noninvasive method may prove useful in preoperative evaluation and postoperative serial assessment of left ventricular wall motion.

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The methods currently used clinically for the assessment of ventricular function are limited in the ability to quantitatively evaluate regional performance. Echocardiography permits noninvasive visualization of regional function but is semiquantitative and highly dependent on both the skills of the sonographer acquiring the images and the judgment of the interpreter. Reproducibility may therefore pose a problem. Nuclear imaging modalities lack resolution on a regional level, although global function can be quantitatively assessed. Because of the increasing focus on techniques and technologies that involve regional intervention, such as anterior ventricular patch reconstruction[1] and cell transplantation,[2,3] there is a need for a noninvasive technique for quantitative assessment of regional function.

Currently used technologies for the prediction of myocardial viability and presumed recoverability in the setting of ischemic heart disease are imprecise.[4] Indeed, positron emission tomography,[5,6] nuclear studies,[7,8] and dobutamine stress echocardiography[9,10] are least accurate in the setting of most severely depressed ventricular function, the very cases in which such prediction is most critical in tailoring surgical therapy to maximize benefit and minimize risk.

There is therefore a need for the development of a noninvasive technique for quantitative assessment of regional ventricular function before and after surgical intervention. Magnetic resonance imaging (MRI) with tissue tagging is an attractive alternative technology. MRI has been used to assess left ventricular (LV) function through analysis of LV wall thickening, ejection fraction, and volumes.[11,12] The high resolution of MRI permits ready delineation of epicardial and endocardial surfaces, and radiofrequency tissue tags within the myocardium serve as landmarks for tracing regional transmural motion.[13] By tracking the movement of discrete points within the myocardium, myocardial strain can be calculated and used to describe quantitatively ventricular wall motion in any given region.[14] Assessment of myocardial strain has the potential to provide reproducible and quantitative information before and after intervention[15] and under resting or stress conditions.[16] We therefore explored the ranges of normal regional myocardial strain from healthy volunteers, characterized global and regional ventricular dysfunction among patients with ischemic coronary artery disease (CAD), and used strain analysis to quantitatively assess serial regional and global changes in ventricular function before and after surgical revascularization for CAD.

Material and Methods

Study Protocol

Patients who had stable CAD and were scheduled for elective CABG were considered for study participation. Exclusion criteria included unstable angina, concomitant valvular disease, and cardiac arrhythmia. Patients underwent MRI before revascularization, with subsequent reimaging at least 3 months after CABG. Preoperative and postoperative results were compared on regional and global bases with control values obtained from a group of 32 healthy volunteers. The study was approved by the Human Studies Committee at Washington University School of Medicine, and informed consent was obtained from each participant before study enrollment.

MRI Acquisition

The imaging technique has been previously described elsewhere.[15] Imaging was performed in a 1.5-T MRI scanner (Siemens Medical Systems, Erlangen, Germany). LV short-axis images were acquired at 8-mm intervals. The midventricular slice (defined as the slice midway between the LV apex and the aortic valve) was chosen for analysis.

With spatial modulation of magnetization, radiofrequency tissue tags were created in an orthogonal grid pattern of presaturation in the myocardium.[14] Sequences of 12 to 18 images were serially acquired through a period of 25 to 40 seconds with the fast low–flip angle shot technique. Image acquisition was electrocardiographically gated and initiated by the R wave of the electrogram, and images were acquired at 29-ms intervals until completion of the cardiac cycle. The end-diastolic image was chosen as the first image in sequence, and the end-systolic image was identified as the image just before ventricular relaxation (smallest ventricular chamber). In all cases the total time required for patient imaging was less than 40 minutes. Imaging parameters included a repetition time of 58 ms per cine-segment, echo time of 2.9 ms, excitation angle of 30°, slice thickness of 8 mm, and a 256 × 256-pixel matrix size. The fields of view were 300 × 300 mm^2 and 400 × 400 mm^2 for the short- and long-axis images, respectively.

Image Processing

Images were analyzed with custom software running on Silicon Graphics workstations (Silicon Graphics, Inc, Mountain View, Calif). Endocardial and epicardial boundaries were manually identified for each image and represented by closed third-order B-spline curves. The initial representation of the tissue tag lines was constructed from the end-diastolic image on the basis of the known spacing (0.78 cm) between adjacent tag lines. Tag lines were located on successive images with an automatic algorithm that was based on local pixel density. Tracking software overlaid a spline for each tissue tag until end-systole was reached. Two-dimensional systolic displacements were computed at each tag line intersection within the myocardium (Figure 1).

Measured and Predicted Displacements

A finite element model of the ventricle was constructed, consisting of six quadrilateral elements corresponding to the anteroseptal, anterior, anterolateral, posterolateral, posterior, and posteroseptal walls. With a least squares fitting model, predicted displacement information was calculated for any point within the myocardium from known measured displacements by a finite element software package (StressCheck; ESRD, St. Louis, Mo). The combination of known and predicted displacement information provided a continuous representation of displacement information for the entire ventricle.[17]

Circumferential Strain Analysis

On a Cartesian coordinate system with the origin defined at the endocardial centroid, the infinitesimal strain tensor *(E)* was computed from displacement information for each point within the model. Briefly, in a two-dimensional system, point displacements in the x and y directions were described by the normal strains e_{xx} and e_{yy}, respectively. The normal strains were computed from the components of displacement as follows:

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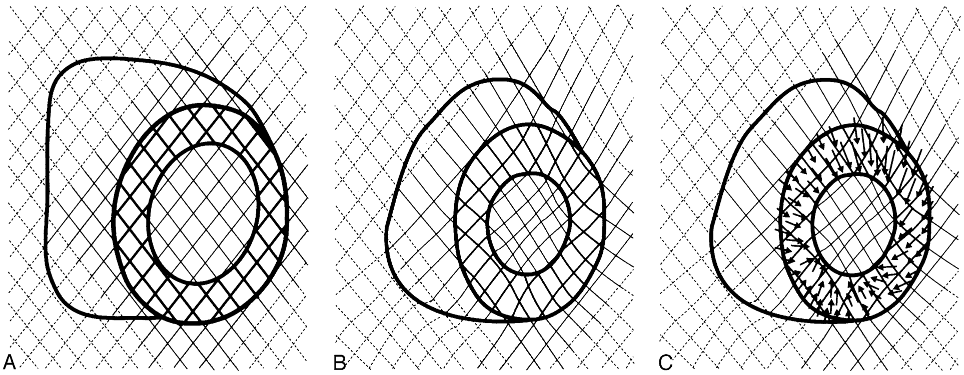

Figure 1. Representation of short-axis MRI of LV at end-diastole (A) and end-systole (B). B-splines are overlaid on tissue tags created in myocardial surface. C, Displacements of points within myocardium are calculated through systole and represented by vectors.

TABLE 1. Demographic data for patients undergoing CABG

Age (y)	60 ± 14
Male (No.)	6 (100%)
Preoperative ejection fraction (%)	47% ± 11%
Two-vessel disease (No.)	1 (17%)
Three-vessel disease (No.)	5 (83%)
No. of bypass grafts	3.8 ± 1.3

$$e_{xx} = \frac{\partial u_x}{\partial x} \quad (1)$$

$$e_{yy} = \frac{\partial u_y}{\partial_y} \quad (2)$$

where u_x and u_y represent the predicted point displacements within the model in the x and y directions.

In the analysis of the cylindric chamber, polar coordinates replaced Cartesian coordinates, and the analysis of motion was done with circumferential strain. Circumferential strain *(CS)* measures the change in point displacement that occurs only within the circumferential direction and was computed as follows:

$$CS = e_{xx} \sin^2\theta + e_{yy} \cos^2 \theta - e_{xy} \sin 2\theta \quad (3)$$

where x and y are related to r and θ by the equations $x = r\cos\theta$ and $y = r\sin\theta$, respectively.[17]

Statistical Methods

The average regional circumferential strain was calculated for each region from values obtained from control subjects (n = 32). Wall segments from patients with CAD were classified as moderately dysfunctional if the regional circumferential strain was more than 2 SD below the normal average strain for that region. A regional circumferential strain more than 3 SD from the normal mean was considered severely abnormal. Comparisons between pre- and post-CABG circumferential strains were done with a 2-tailed paired Student *t*, test with patient serving as their own controls. Unless otherwise specified, data are presented as mean ± SD. When required, multiple comparisons were performed with a 1-way analysis of variance with repeated measures.

Results

Control Subjects

Thirty-two volunteers (17 male) without known cardiac disease underwent resting MRI. The average age was 29.5 ± 7.7 years. The regional circumferential strain in control subjects was greatest for the lateral segments (anterolateral, posterolateral) versus the anterior, posterior, anteroseptal, and posteroseptal walls ($P < .001$; Figure 2). Circumferential strain among volunteers followed a normal distribution, with minimal variability within any given wall region (SD 0.04-0.05).

Study Patients

Six male patients with multivessel CAD and stable angina pectoris were enrolled in the study (Table 1). Preoperative MRI was performed a median of 7.5 days (range 3-59 days) before CABG. Postoperative MRI was performed an average of 188 ± 103 days after CABG. A discrete wall motion abnormality was identified by left ventriculography in 5 of 6 patients. Preoperative echocardiography was performed in 3 of the 6 patients, and results of preoperative thallium single-photon emission computed tomographic (SPECT) viability studies were available for 4 of the 6 patients. All patients had complete revascularization, with an average of 3.8 ± 1.3 grafts per patient.

Preoperative Circumferential Strain Analysis

Regional analysis by circumferential strain identified 15 segments with normal function (within 2 SD of normal), 8 segments as moderately dysfunctional (outside 2 SD of normal), and 13 severely dysfunctional wall segments (outside 3 SD of normal; Figure 3). Three segments demonstrated no shortening at all within the circumferential direction (circumferential strain of 0 or less). The average

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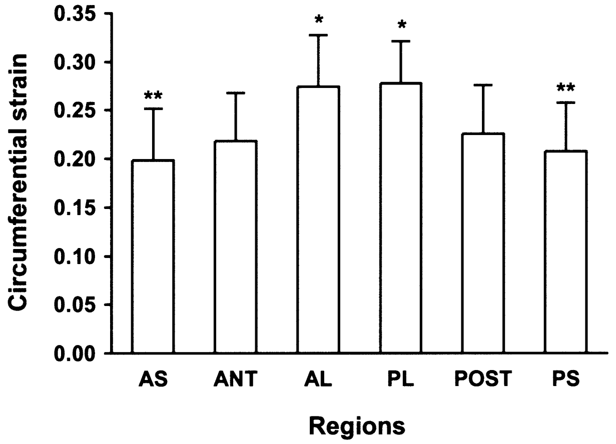

Figure 2. Regional circumferential strain from control subjects. *Asterisks* indicate regional circumferential strain significantly greater for lateral walls (anterolateral, posterolateral) than for anterior *(ANT)* and posterior *(POST)* walls ($P < .001$). *Double asterisks* indicate circumferential strain for either septal wall (anteroseptal, posteroseptal) significantly less ($P < .001$) than for any other wall (anterior, posterior, anterolateral, posterolateral). There was minimal variability within any given region (SD 0.04-0.05). *AS,* Anteroseptal; *AL,* anterolateral; *PL,* posterolateral; *PS,* posteroseptal.

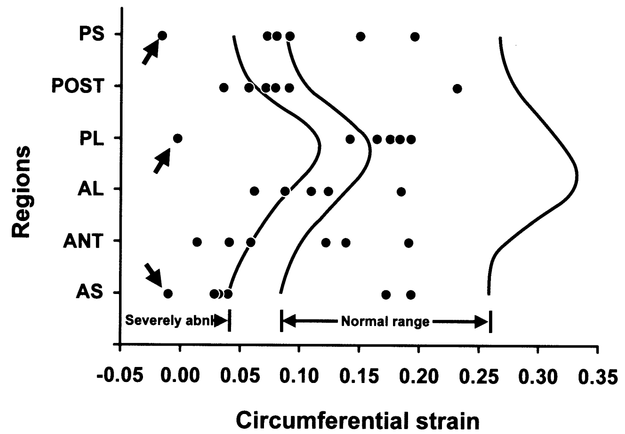

Figure 3. Regional circumferential strain among ischemic patients before CABG. Circumferential strain is represented along x-axis, beginning with severely abnormal to normal. Each *data point* represents preoperative region among ischemic patients. Depressed circumferential strain accounted for 64% of ventricular regions (23/36). Three segments failed to produce any circumferential shortening *(arrows)* and had circumferential strain of 0 or less. *PS,* Posteroseptal; *POST,* posterior; *PL,* posterolateral; *AL,* anterolateral; *ANT,* anterior; *AS,* anteroseptal.

TABLE 2. Regional comparison of preoperative LV wall motion by echocardiography and circumferential strain analysis

Case		Anteroseptal	Anterior	Anterolateral	Posterolateral	Posterior	Posteroseptal	Global
2	Echocardiography	D	D	D	D	D	D	D
	Circumferential strain	D	N	D	D	D	D	D
3	Echocardiography	D	N	N	N	N	N	D
	Circumferential strain	D	D	N	D	N	D	D
6	Echocardiography	N	N	N	N	N	N	N
	Circumferential strain	N	N	N	N	D	N	N

D, Dysfunctional; *N,* normal.

number of severely dysfunctional segments identified by circumferential strain was 2.5 segments per patient. Global circumferential strain in patients with CAD was significantly depressed relative to that in the control group (0.11 ± 0.05 for ischemic group vs 0.20 ± 0.03 for control group, $P < .001$).

Correlation with conventional indices. All segments in patients with CAD identified as dysfunctional by preoperative ventriculography (hypokinetic to dyskinetic, n = 10) had depressed strains according to circumferential strain analysis. Eight of these 10 regions had severely depressed circumferential strain (outside 3 SD). Echocardiographic data were available for 3 patients. Regionally, circumferential strain results matched echocardiographic findings for 13 of 18 segments. Strain analysis identified all but 1 dysfunctional region. Four segments had circumferential strain that were dysfunctional (>2 SD below the mean) but showed normal wall motion on echocardiography (Table 2). Global circumferential strain correlated with all 3 ejection fractions determined by echocardiography.

Global circumferential strain correlated with preoperative ejection fraction by contrast ventriculography in the right anterior oblique projection with an r value of 0.84 ($P < .01$; Figure 4). The single outlier with a higher ejection fraction than expected from circumferential strain had a marked lateral wall motion abnormality on MRI that was not apparent on ventriculography in the right anterior oblique projection.

Postoperative Circumferential Strain Analysis

The number of regions with normal circumferential strain increased from 15 to 21, and the number of severely abnormal segments decreased from 13 to 5 (Figure 5). Each patient demonstrated increased circumferential strain in at

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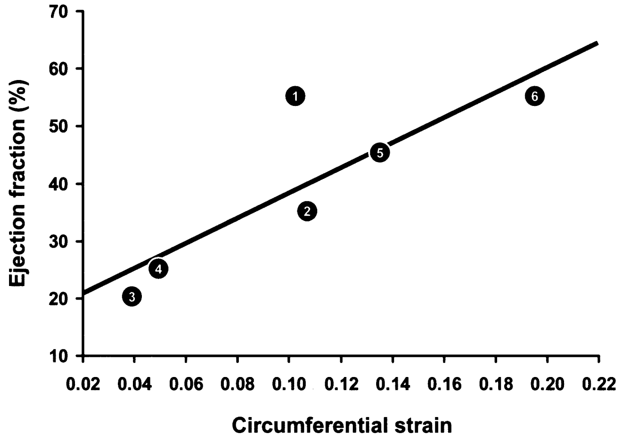

Figure 4. Correlation of ejection fraction and global circumferential strain. Preoperative ejection fraction, as determined by ventriculography in right anterior oblique projection, demonstrated linear relationship with global circumferential strain obtained from tissue-tagged MRI (r = 0.84, P < .01).

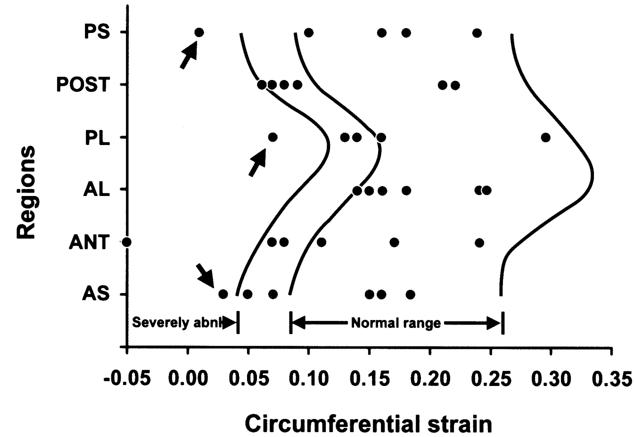

Figure 5. Regional circumferential strain among ischemic patients after CABG. Circumferential strain is represented along x-axis beginning with severely abnormal *(abnl)* to normal. After CABG, number of regions with depressed circumferential strain decreased to 36% (13/36). Number of severely abnormal segments decreased from 13 to 5. *Arrows* represent same 3 preoperative segments that had circumferential strain of 0 or less. *PS,* Posteroseptal; *POST,* posterior; *PL,* posterolateral; *AL,* anterolateral; *ANT,* anterior; *AS,* anteroseptal.

least 1 segment. Overall, global circumferential strain demonstrated significant improvement in the ischemic group after CABG relative to preoperative circumferential strain (0.11 ± 0.05 vs 0.14 ± 0.05, P = .007; Figure 6). One patient with abnormal global strain did not have postoperative improvement.

Viability Testing

The postoperative changes in circumferential strain correlated with preoperative viability testing with SPECT imaging in all 4 cases for which the data were available. All fixed defects predicted by preoperative SPECT imaging (n = 4) had minimal improvement of postoperative circumferential strain and remained dysfunctional. All ischemic defects predicted by SPECT imaging regained circumferential strain within the normal range determined from the control subjects.

Discussion

The results of this study support the further investigation of MRI with tissue tagging as a clinically applicable means of quantitatively assessing regional ventricular wall motion. Our findings demonstrated that patients with CAD had depressed circumferential strain both regionally and globally relative to control subjects. Although other strain components, such as radial, longitudinal, and minimal principle strain, have been investigated, we chose to focus on the circumferential component because of the previous work of others demonstrating the predictability of this measure in normal and ischemic tissues.[18-20] Our preoperative circumferential strain results are consistent with previous studies, and we also demonstrated improved circumferential strain after surgical revascularization.

Circumferential strain calculations for patients with normal LV function had little variability within a given segment from patient to patient, but there were significant differences in the observed circumferential strain between regions, such as the septum versus the lateral walls. These differences between segments are not unexpected, given the relationships between the LV wall and other structures. For instance, one would anticipate an impact of right ventricular attachment and intraventricular pressure on the wall motion observed in the septum. The pattern of increased circumferential strain in the lateral walls is consistent with findings in healthy volunteers observed in several other investigations.[13,18-22]

Previous animal studies have shown good correlation of MRI with invasively placed sonometric instrumentation in the evaluation of wall motion.[23] Clinically, circumferential strain calculations have already been shown to be reproducible[24] and to demonstrate high sensitivity for detecting changes in ventricular motion after acute myocardial infarction.[19,25,26] Additionally, MRI with strain analysis has been used to predict myocardial recovery after myocardial infarction.[27,28] This study now extends this technology to quantitative assessment of LV wall motion before and after CABG.

Although data were not available for all patients, the agreement between SPECT-assessed viability and postoperative circumferential strain improvement was consistent. Of interest were the 3 segments that failed to demonstrate any circumferential shortening by circumferential strain analysis before the operation. Preoperative strain analysis indicated overall regional lengthening during systole. The absence of motion within the circumferential direction for these segments is consistent with myocardial scar, and appropriately all 3 segments failed to show any significant postoperative improvement. All patients in this study demonstrated various levels of regional improvement. In addition, global circumferential strain was within normal limits for 4 of the 6 patients, and although it had not normalized, it had improved substantially for another patient. The failure to demonstrate a significant improvement for the remaining patient was consistent with preoperative SPECT but may also reflect the limitation of the 2-dimensional analysis and its inability to capture the entire ventricle.[29] It has also been suggested that patients with significantly depressed ventricular function may need longer follow up (>3 months) to allow for further recovery.[30,31]

Although the finding that LV function generally improves after CABG is not novel, the ability to serially quantify postoperative changes with this degree of resolution may have significant clinical utility. Quantitative methodologies have the potential to provide an objective index and replace the qualitative assessments performed by routine angiography or echocardiography.[32,33] This may improve the accuracy and therefore comparability of serial patient examinations and those performed by different clinicians and at separate institutions.[34] Semiquantitative MRI is already being used at some centers for clinical evaluation of patients after cardiac transplantation.[35] The quantitative nature of tissue tagged MRI with circumferential strain analysis particularly lends itself to objective assessments of the myocardium that require multiple examinations. For example, determining viability or recoverability of infarcted myocardium through pharmacologic stress before CABG, mapping the mechanics of LV function after reconstructive surgery for LV aneurysm, measuring the effects of cell transplantation on LV wall motion, and assessing angiogenic therapies in the treatment of CAD are all treatment modalities currently being investigated that could benefit from a quantitative, noninvasive modality to assess LV wall motion.

Limitations

This study was principally limited by the relatively small size of the ischemic group. A second limitation was that the normal range of circumferential strain was obtained from a relatively younger population. Although the mean age of subjects used to establish normal ranges was significantly lower than that of our surgical study group, previous work has shown changes in chamber shapes, volumes, and mass with no change or a relatively slight decline in ventricular function with normal aging.[36-38] Future efforts in our laboratory will be directed to accruing more data on healthy individuals of more advanced age. The third limitation was that the 2-dimensional analysis used in this study cannot account for through-plane motion. The MRI technology used in this study is, however, amenable to 3-dimensional analysis by creating tissue tags on long-axis images. Progress toward 3-dimensional analysis is currently underway.

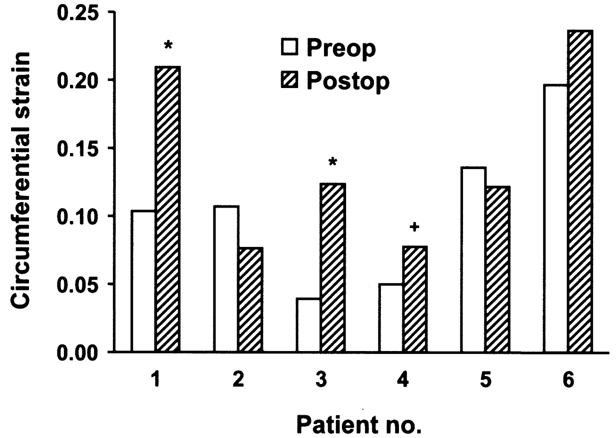

Figure 6. Global circumferential strains before *(Preop)* and after *(Postop)* CABG. *Asterisks* indicate postoperative global circumferential strain improved significantly ($P < .02$). *Plus sign* indicates postoperative global circumferential strain trended toward significance ($P = .09$). Postoperative circumferential strain for patients 1, 3, 5, and 6 was consistent with regained normal LV wall motion.

Summary

Circumferential strain provided an objective LV wall motion assessment that was consistent among healthy volunteers in this study and with reports from other investigators. Serial measurements of circumferential strain characterized the ventricular dysfunction in patients with CAD and correlated with conventional tools for myocardial assessment. Postoperative improvements in circumferential strain were consistent with viability testing and successfully identified changes in regional and global ventricular wall motion after CABG in this patient subset.

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